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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,140	11/18/2003	Dean L. Engelhardt	Enz-52(C)(D3)	7276

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	
MAIL DATE	DELIVERY MODE
10/18/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,140	ENGELHARDT ET AL.	
	Examiner	Art Unit	
	FRANK W. LU	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *91,93-102,104,110-119 and 122-129* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *91,93-102,104,110-119 and 122-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/16/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of species (2) (said promoter is a bacteriophage promoter, see claims 124, 126, and 128) and species (4) (said polymerase is a bacteriophage RNA polymerase, see claims 125, 127, and 129) in the reply filed on July 22, 2010 is acknowledged. The traversal is on the ground(s) that: (1) "[A]t the outset, Applicants respectfully submit that the various members recited in previously added claims 124-129 clearly represent a reasonable number of species (only two!) which are permitted under U.S. patent law. Examination of both members represented by the conjugates of claims 124-129 will not impose a harsh or undue burden on either the search for prior art or in the examination of this application in light of any prior art that may be uncovered. Applicants believe that many of the above-named species are recited in the same claim or claims of issued U.S. patents. See, for example, Polo et al., U.S. Patent No. 6,242,259 (claim 53 'wherein said promoter is a eukaryotic promoter' and claim 54 ('wherein said promoter is a bacteriophage promoter'); and Polo et al., U.S. Patent No. 6,329,201 (claim 7 'wherein said promoter is a eukaryotic promoter;' and claim 8 ('wherein said promoter is a bacteriophage promoter')"; and (2) "[A]pplicants believe that one or more of the currently named inventors continue to be an inventor of at least one claim in the pending claims, including claims 124-129 which are the subject of this species election. No amendment of inventorship is believed, therefore, to be required or necessary".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the restriction requirement nor persuasive toward the relaxation of same such that species (1) to (4) will be examined together. First, applicant has no evidence to

show there is no search burden for searching species (1) to (4) together. In fact, there is a search burden on the examiner to search species (1) to (4) together. For example, searching for species (1) such as eukaryotic promoter is not required for species (2) while searching for species (2) such as bacteriophage promoter is not required for species (1) and searching for species (3) such as eukaryotic RNA polymerase is not required for species (4) while searching for species (4) such as bacteriophage RNA polymerase is not required for species (3). Second, according to the Election of Species mailed on June 9, 2010, "[S]hould applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case". However, applicant has not submitted evidence to show species (2) is an obvious variant of species (1) and species (4) is an obvious variant of species (3). Third, although, in U.S. Patent No. 6,242,259, claim 53 contains "wherein said promoter is a eukaryotic promoter" and claim 54 contains "wherein said promoter is a bacteriophage promoter", while, in U.S. Patent No. 6,329,201, claim 7 contains "wherein said promoter is a eukaryotic promoter" and claim 8 contains "wherein said promoter is a bacteriophage promoter", applicant has no evidence to show that eukaryotic promoter is an obvious variant of eukaryotic promoter. In the above reasons and in the absence of convincing evidence to the contrary, the election of species requirement has been maintained and is hereby made final. However, the examiner agrees to combine species (1) and (3) with species (2) and (4) when the claims are allowable. Claims 91, 93-102, 104, 110-119, and 122-129 will be examined.

Claim Objections

2. Claim 91 or 110 or 119 is objected to because of the following informality: "a eukaryotic cell" in the preamble should be "an eukaryotic cell".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Scope of Enablement

Claims 91, 93-102, 104, 110-119, and 122-129 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing a specific RNA comprising a sequence coding for a protein in an eukaryotic cell *in vitro* by introducing a conjugate formed by a RNA polymerase and a vector containing a promoter for the RNA polymerase and a DNA comprising a sequence coding for the protein wherein the promoter for the RNA polymerase is upstream of said DNA comprising a sequence coding for the protein (ie., using said conjugate) and said RNA polymerase is covalently linked to the promoter, does not reasonably provide enablement for producing a specific RNA recited in claims 91, 93-102, 104, 110-119 and 122-129 in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91, 93-102, 104, 110-119 and 122-129 into the cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

Claims 91, 93-102, 104, 110-119 and 122-129 are directed to a conjugate. The invention is a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.,* 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth of The Claims

Claims 91-102, 104, 124, and 125 encompass a conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of a specific RNA comprising a sequence coding for a protein and a RNA polymerase cognate to said promoter wherein, when said conjugate is introduced into an eukaryotic cell *in vitro*, the conjugate can produce said specific RNA and said RNA polymerase is covalently linked to said nucleic acid of said protein-nucleic acid construct. Claims 110-118, 126, and 127 encompass a conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one segment of a specific RNA, and a RNA polymerase cognate to said promoter wherein, when said conjugate is introduced into an eukaryotic cell *in vitro*, said conjugate produces said specific

RNA and said RNA polymerase is covalently linked to said nucleic acid of said protein-nucleic acid construct. Claims 119, 122, 123, 128, and 129 encompass a conjugate comprising a protein-nucleic acid construct that comprises at least one promoter, at least one single-stranded RNA segment comprising a sequence complementary to any kind of primer present in an eukaryotic cell and a RNA polymerase cognate to said promoter wherein, when said conjugate is introduced into said cell *in vitro*, the conjugate can produce a specific RNA and said RNA polymerase is covalently linked to said nucleic acid of said protein-nucleic acid construct.

Working Examples

The specification provides working examples (see pages 43-63) for amplification of different DNAs and amplification from RNA template. The specification provides no working example for producing a specific RNA recited in claims 91, 93-102, 104, 110-119 and 122-129 in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91, 93-102, 104, 110-119 and 122-129 into the cell.

The Amount of Direction or Guidance Provided and The State of The Prior Art

Although the specification teaches a protein- nucleic acid complex formed by M13mp18 RF and DNA polymerase (see Example 3, pages 45 and 46), the specification does not provide a guidance for producing a specific RNA recited in claims 91-102, 104, 110-119, and 122-129 in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91-102, 104, 110-119, and 122-129 into the cell. Furthermore, there is no experimental condition and/or experimental data in the specification to support the claimed invention. Although it is known in the art that T7 RNA polymerase RNA can be produced in a cell *in vitro* when a conjugate formed by T7 RNA

polymerase and a vector containing T7 promoter and T7 RNA polymerase gene is introduced into the cell *in vitro* wherein T7 RNA polymerase gene is controlled by T7 promoter in the vector (see Wagner *et al.,* US Patent No. 5,591,601, see abstract, columns 2, 3, and 5), during the process of the prior art search, the examiner has not found any art which is related to produce a specific RNA recited in claims 91-102, 104, 110-119, and 122-129 in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91-102, 104, 110-119, and 122-129 into the cell.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether a specific RNA recited in claims 91-102, 104, 110-119, and 122-129 can be produced in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91-102, 104, 110-119, and 122-129 into the cell. Since it is known that RNA polymerase is used for synthesis RNA during transcription and the transcription includes initiation, elongation and termination, and begins with the binding of RNA polymerase to the promoter in the gene (DNA) which is located on the upstream of the gene (see attached definition for "transcription" from Wikipedia, the free encyclopedia) and the claims do not require that the nucleic acid in the protein-nucleic acid is DNA and the at least one promoter is upstream of the nucleic acid in the protein-nucleic acid, if the nucleic acid in the protein-nucleic acid is RNA, it is unclear how a specific RNA recited in claims 91-102, 104, 110-119, and 122-129 can be produced in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91-102, 104, 110-119, and 122-129 into the cell. Furthermore, since the claims does not require

that said RNA polymerase is covalently to the promoter and it is known that the transcription begins with the binding of RNA polymerase to the promoter in the gene which is located on the upstream of the gene (see attached definition for "transcription" from Wikipedia, the free encyclopedia), if said RNA polymerase is not covalently to the promoter but is covalently to the nucleic acid in the protein-nucleic acid, it is unclear how the transcription of a specific RNA can be initialed so that the specific RNA recited in claims 91-102, 104, 110-119, and 122-129 can be produced in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91-102, 104, 110-119, and 122-129 into the cell.

In view of above discussions, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether a specific RNA recited in claims 91-102, 104, 110-119, and 122-129 can be produced in an eukaryotic cell *in vitro* by introducing the conjugate recited in claims 91-102, 104, 110-119, and 122-129 into the cell.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high, the specification provides one with no guidance that leads one to claimed methods. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working example related to the invention and the no teaching in the prior art balanced only

against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

5. Applicant's arguments with respect to claims 91-102, 104, 110-119, 122, and 123 have been considered but are moot because, although some issues listed in the rejection under 35 U.S.C. 112, first paragraph in the office action mailed on August 19, 2009 have been removed in view of the applicant's arguments and the amendment, the applicant has not argued all issues listed in the rejection under 35 U.S.C. 112, first paragraph in the office action mailed on August 19, 2009. Above rejection under 35 U.S.C. 112, first paragraph in this office action is based on the issues in the rejection under 35 U.S.C. 112 in the office action mailed on August 19, 2009 which have not been argued by applicant.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. No claim is allowed.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen, can be reached on (571)272-0731.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Frank W Lu /
Primary Examiner, Art Unit 1634
October 12, 2010